-- Figures 1A and 1B provide genomic sequence (SEQ ID NO:1) from the DPD gene in the region of a splicing mutant which leads to the loss of an exon in the mRNA which encodes amino acids 581-635 (SEQ ID NO:2). The primer binding sites for DELF-1 (SEQ ID NO:3) and DELR1 (SEQ ID NO:4) are indicated. The primer binding site for DPD15F (SEQ ID NO:5) and DPD15R (SEQ ID NO:6) (*see*, Meinsma *et al.* (1995) *DNA and Cell Biology* 14(1): 1-6) are also indicated. The Mae II site at the 3' splice junction is indicated. In a mutant form, the G nucleotide at the 3' splice junction (residue 434) is mutated to an A nucleotide.

a2

Figure 2 provides further details of PCR reaction components for amplifying the region of a splicing site mutant (SEQ ID NO:7) The exon is underlined. The splice site which is polymorphic is in bold text. Primers DELF1 and DELR1 are indicated (SEQ ID NOS:3 and 4) --

Please replace the paragraph beginning at page 21, line 23, with the following rewritten paragraph:

-- The PCR primers were selected so as to bracket the exon that is not present in the DPDD gene and part of the two introns on either side of this exon. Primers were synthesized using an Applied Biosystems 394 DNA & RNA synthesizer. The forward primer was DELF1, which encompassed nucleotide 154 to nucleotide 175 of the DPDD gene sequence and had the sequence TGCAAATATGTGAGGAGGGACC (SEQ ID NO: 3) (*see also* Figure 1 and Figure 2). The reverse primer was DELR1, which encompassed nucleotide 563 to nucleotide 542 of the DP[F]DD gene sequence and had the sequence CAAAGCAACTGGCAGATTC (SEQ ID NO: 4) (*see also* Figure 1 and Figure 2). PCR was carried out in 50 µl of a reaction mixture consisting of 10 m*M* Tris-HCl pH 8.3, 50 m*M* KCl, 2.5 m*M* $MgCl_2$, 0.5 m*M* dNTPs, 1 µ*M* of each primer, and 2.5 units *Taq* polymerase (Roche Molecular Systems) for 30 cycles denaturing at 96°C for 1 min, annealing at 55°C for 1 min, and extending at 72°C for 2 min. The amplified products were extracted with 1 volume of chloroform and purified by filtration through Centricon 100 filter units. --

a3

Please replace the paragraph beginning at page 23, line 29, with the following rewritten paragraph:

-- The DPD cDNA was used as a probe to isolate a P1 clone containing about 100 kbp of the human *DPD* gene (PAC 5945) from a high density PAC human genomic library (Genome

a4

Systems, St. Louis, MO). Southern blotting was used to confirm that the P1 clone contained the deleted exon using a probe located within the deleted fragment. This probe was synthesized from the DPD cDNA by using the primers: DPD15 (forward): 5' TTGTGACAAATGTTTCCC 3' (SEQ ID NO: 5) and DPD15R (reverse): 5' AGTCAGCCTTTAGTTCAGTGACAC 3' (SEQ ID NO: 6) to specifically amplify the putative exon. PCR conditions were as indicated below but extension was carried out at 72°C for 1 min. This PCR fragment was purified using a Wizard PCR purification kit (Promega, Madison, WI), labeled with [α^{32}P]-dCTP and hybridized with the clone PAC 5945. DNA was purified from this genomic clone using Qiagen columns (Qiagen, Chatsworth, CA), and the 5' and 3' end of the deleted exon and adjacent intronic regions were sequenced by chromosome walking from within the deleted exon using dideoxy terminator chemistry and an ABI 373A DNA sequencer (Applied Biosystems, Foster City, CA). The intronic sequences obtained allowed the selection of appropriate primers (*e.g.*, delF1 and delR1) to amplify from genomic DNA the complete exon and immediate flanking intronic sequences. All primers used in this study were synthesized with a 391 DNA&RNA synthesizer (Applied Biosystems, Foster City, CA). --

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Please replace the paragraph beginning at page 24, line 16, with the following rewritten paragraph:

-- A 409 bp PCR genomic fragment corresponding to the deleted exon (from G1822 to C1986 in Yokota, *et al.* (1994) *J. Biol. Chem.* 269: 23192-23196) plus the flanking intronic sequences containing the AG and GT splicing consensus sequences was amplified from human genomic DNA using the primers delF1 (forward) 5' TGCAAATATGTGAGGAGGGACC 3' (SEQ ID NO: 3) and delR1 (reverse) 5' CAGCAAAGCAACTGGCAGATTC 3' (SEQ ID NO: 4). PCR amplification was carried out in a 100 µl reaction mixture containing 10 mM Tris-HCl (pH 8.3), 50 mM KCl, 1.5 mM $MgCl_2$, 0.2 mM of each dNTP, 0.5 µM of each primer, 2.5 units of *Taq* Polymerase (Roche Molecular Systems) and 500 ng of genomic DNA template for 31 cycles by denaturing at 94°C for 1 min, annealing at 60°C for 1 min and extending at 72°C for 2 min. Subjects identified as wild type, heterozygous or homozygous for the splicing mutation could be distinguished by digesting the PCR product with the restriction endonuclease Mae II (Boehringer, Mannheim, Indianapolis, IN) and electrophoresis in 1% regular, 3% NuSieve agarose gels (FMC Bioproducts, Rockland, ME). The genotypes obtained were verified by sequencing the 409 bp PCR